REMARKS

Status of the Claims

Claims 1-7, 9-17, 19-28, 30-38, 40-49, 51-59, and 61-65 are pending and under examination.

Claims 11, 12, 16, 32, 33, 37, 53, 54, and 58 are amended herein.

Applicants reserve the right to reintroduce cancelled subject matter, for example, in a later-filed continuing application

No new matter is introduced by the present amendment.

Rejections under 35 U.S.C. § 112-2nd are Rendered Moot

The Examiner rejected Claims 11, 12, 16, 32, 33, 37, 53, 54, and 58 as allegedly indefinite.

According to the Examiner, '[t]he phrase "greater than" however, is contraverted by the term "about" ...' Office Action at page 2, No. 5A and page 3, Nos. 5B and 5C.

Although Applicants believe that previous claim language is not indefinite, in order to advance prosecution, Applicants have amended Claims 11, 12, 16, 32, 33, 37, 53, 54, and 58 to delete "about."

Accordingly, any asserted basis for the rejection is now rendered moot, and Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. §103(a) are traversed

Fairman Reference

The Examiner rejected Claims 1-7, 9-16, 19-28, 30-37, 40-49, 51-58, and 61-65 under 35 U.S.C. §103(a) as allegedly being obvious over Fairman (US 2002/0068280 A1; cited in a previous Office Action).

According to the Examiner, "Fairman does not teach adding the high salt solution which precipitates the DNA before lysing the cells. However, it would have been *prima facie* obvious

to one of ordinary skill in the art to have reversed the steps of adding a high-salt solution before cell lysis. As stated in several Court decisions, changing the order of steps is *prima facie* obvious (see MPEP 2144.04.IV.C) ..." Office Action at page 6, lines 3-7.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP §2143. It is well established that failure to meet any one of these criteria negates a finding of *prima facie* obviousness.

Prima facie obviousness in the present instance is negated at least because Fairman does not teach or suggest all the claim limitations. More specifically, Fairman at least does not teach or suggest contacting a biological material comprising DNA with a hypertonic, high salt reagent. Moreover, Fairman does not teach or suggest contacting a biological material comprising DNA with a hypertonic, high salt reagent so as to form a suspension of said biological material containing DNA.

Applicants respectfully disagree with the Office assertion that "since the second [aqueous] solution of [Fairman] contains salt concentration of about 200-300 mM, it is a hypertonic solution." Office Action at page 4, last two lines; [emphasis added]. Although the Office asserts that the second [aqueous] solution contains salt concentration of about 200-300 mM *[Office states: it is Applicant's understanding that the assertion is based on the disclosure by Fairman at ¶[0026], lines 8-10 regarding the molarity of the first aqueous solution in view of ¶[0030], lines 1-3 and lines 22-26 that describes the second aqueous solution as being "the same as" (or having "similar osmotic pressure, ionic strength and pH") as the first aqueous solution]*, the Office mischaracterizes such a solution [containing a salt concentration of about 200-300 mM] as hypertonic.

For example, according to Fairman, a solution containing a salt concentration of about 200-300 mM lyses red blood cells. See, *e.g.*, Fairman at ¶[0026] at least at lines 10 and 14-15. And, as evidenced by US Patent No. 5,777,098 to Gray *et al.*, which is of record (see Office Action dated July 15, 2007 at page 10, No. 6A),

> The method of the present invention comprises a first step of gently lysing the membranes of the red blood cells (non-DNA containing cells) in the biological sample. Lysis herein is the physical disruption of the membranes of the cells. This

> first step utilizes a hypotonic solution which causes the cell fluids to enter the cell, thereby causing the cell membranes to rupture.

See, e.g., US5,777,098 to Gray *et al.*, Col. 3, lines 5-7; [emphasis added]. Thus, a solution containing a salt concentration of about 200-300 mM for lysing red blood cells is hypotonic (and not, as the Office asserts, a hypertonic). Moreover, Applicants' disclosure teaches that "[t]ypical suspension solutions are hypotonic, such as that used in a pretreatment step to [lyse] red blood cells in mammalian blood." Published App. 2003/0157492 at page 1, paragraph [0002], lines 13-16. Thus, the Office's characterization of Fairman's second [aqueous] solution [e.g., containing a salt concentration of about 200-300 mM] as hypertonic is incorrect. Accordingly, Fairman at least does not teach or suggest contacting a biological material comprising DNA with a hypertonic, high salt reagent.

Moreover, Fairman teaches contacting a cell lysate with a fourth aqueous solution (*e.g.*, 5M ammonium acetate) to precipitate proteins. Accordingly, Fairman does not teach or suggest contacting a biological material comprising DNA with a hypertonic, high salt reagent so as to form a suspension of said biological material containing DNA.

Moreover, the Office assertion that "it would have been *prima facie* obvious to one of ordinary skill in the art to have reversed the steps of adding a high-salt solution before cell lysis" is misplaced because, as pointed out above, Fairman does not teach or suggest all the claim limitations.

Even assuming, *in arguendo*, that the Office is correct in its assertion that "Fairman does not teach adding the high salt solution which precipitates the DNA before lysing the cells" but "it would have been *prima facie* obvious to one of ordinary skill in the art to have reversed the steps of adding a high-salt solution before cell lysis," secondary considerations, or indicia of nonobviousness, such as Applicants' unexpected findings rebut a *prima facie* case of obviousness. MPEP §716.01(a). Applicants' unexpected findings are evidence of nonobviousness. *Graham v. John Deere, Co. of Kansas City*, 383 U.S. 1 (1966).

Applicants' invention teaches unexpected findings. Published App. 2003/0157492 at page 1, paragraph [0007], lines 8-9. Applicants teach unexpected findings such as reducing the overall time, number of steps and reagents required for isolating DNA. See, *e.g.*, Published App.

2003/0157492 at page 1, paragraph [0007]; Example 1, Comparison of Standard Method to New Rapid method; and, paragraph [0044] at page 6-7. By way of example with reference to isolating DNA from blood cells, at page 4, paragraph [0023] of the published Application, Applicants state,

> The methods of DNA isolation disclosed in the prior art employ a lysis reagent before the addition of a protein precipitation step. However, the current invention discloses a novel method in which a hypertonic, high-salt reagent is added first, followed by the addition of a lysis reagent. The hypertonic, high-salt reagent unexpectedly causes the white blood cells to resuspend in solution without the commonly encountered problems of aggregation or clumping. Thus, the hypertonic, high-salt reagent is used to resuspend the material as well as precipitate protein contaminants, which is its normal function. The hypertonic, high-salt reagent in this procedure thus serves three purposes 1) to resuspend the biological material, eliminate aggregation and clumping, and thus facilitate efficient cell lysis; 2) to reduce RNA contamination; and 3) to remove contaminants (for example, proteins) in the presence of detergent, which is its normal function. [emphasis added]

Thus, one of ordinary skill in the art would recognize the surprising result that, having carried out the steps of the present invention, there is rapid resuspension without significant damage to the sample and no need for any further physical dispersion steps. Applicants' method is disclosed at least in Example 1 with reference to white blood cells treated by the steps of the present invention ("Rapid Method") compared with a Standard Method, but as mentioned at page 5, paragraph [0028] lines 13-18, the application of the invention goes beyond blood cells.

Thus, at least Applicants' unexpected findings rebut the Office's assertion that Applicants' invention is obvious.

Accordingly, *prima facie* obviousness in the present instance is negated at least because Fairman does not teach or suggest all the claim limitations. Moreover, even assuming, *in arguendo*, that a *prima facie* case of obviousness had been made, secondary considerations, such as Applicants' unexpected findings, rebut a *prima facie* case of obviousness. MPEP §716.01(a).

Therefore, Applicants respectfully request that the Examiner withdraw the rejection.

Fairman and Hanak et al. References

The Examiner rejected Claims 17, 38, and 59 under 35 U.S.C. §103(a) as allegedly being obvious over Fairman (US 2002/0068280 A1; cited in a previous Office Action) and Hanak et al. (U.S. Patent No. 6,780,632).

The Office states, "[t]he teachings of Fairman et al. are presented above. The reference does not teach using RNAse in the purification protocol." Office Action at page 6, No. 9A. And, the Office states, "Hanak et al. teach preparing RNA-free DNA using RNAse (Abstract; col. 2, lines 30-35; col. 35, lines 46-47; col. 36; col. 37; col. 38, lines 1-44)." Office Action at page 6, No. 9B, lines 1-2. According to the Office, "[i]t would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used RNAse of Hanak et al. in the DNA preparation method of Fairman. The motivation to do so, provided by Hanak et al., is that RNA is a major contaminant of preparations of genomic and plasmid DNA from cell lysates (col. 1, lines 36-50)." Office Action at page 6, last two lines through page 7, lines 1-2.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP §2143. It is well established that failure to meet any one of these criteria negates a finding of *prima facie* obviousness.

Prima facie obviousness in the present instance is negated at least because Fairman and Hanak et al., alone or when combined, do not teach or suggest all the claim limitations. More specifically, Fairman and Hanak et al. at least do not teach or suggest contacting a biological material comprising DNA with a hypertonic, high salt reagent. Moreover, neither reference, alone or when combined, teaches or suggests contacting a biological material comprising DNA with a hypertonic, high salt reagent so as to form a suspension of said biological material containing DNA. And, neither reference, alone or when combined, teach or suggest a lysis reagent containing RNAse solution.

Applicants restate the discussions above as they relate to Fairman. And, the Office concedes that "[t]he reference does not teach using RNAse in the purification protocol." Office Action at page 6, No. 9A.

Hanak et al. fails to cure the defects of Fairman. Hanak et al. at least do not teach contacting a biological material comprising DNA with a hypertonic, high salt reagent. Moreover, the reference does not teach or suggest contacting a biological material comprising DNA with a

hypertonic, high salt reagent so as to form a suspension of said biological material containing DNA.

Moreover, Hanak et al. do not teach or suggest contacting a suspension of biological material containing DNA with a lysis reagent containing RNAse solution. Hanak et al. teaches away from a lysis reagent containing RNAse at least because, according to the reference, "there are limitations to using exogenously produced RNAses." Hanak et al., Col. 1, lines 64-65; [emphasis added]. For example, Hanak et al. states, "[t]he most significant limitation to using exogenously produced RNase is that, if the exogenously added RNase is of animal origin, following RNase treatment the presence of residual enzyme can contaminate a DNA preparation, thereby rendering it unacceptable for certain applications ..." Hanak et al., Col. 2, lines 10-15; [emphasis added]. According to the reference, "[t]here is a need in the art for a method of removing RNA from cellular components that does not rely on incubating a cellular lystate or purified component with added exogenously produced RNase." Hanak et al., Col. 2, lines 23-27; [emphasis added]. The reference teaches lysing cells that produce the cellular component of interest to produce a cell lysate, wherein the cell lysate contains sufficient RNase activity. Hanak et al., Col. 2, lines 30-36. For example, according to the reference, the RNase is produced by the same cell producing the cellular component or by cells in the medium other than those cells producing the cellular component. Hanak et al., Col. 2, lines 30-41.

Thus, *Prima facie* obviousness in the present instance is negated at least because Fairman and Hanak et al., alone or when combined, do not teach or suggest all the claim limitations. Therefore, Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

Applicants believe these Remarks place the claims in condition for allowance and such action is respectfully requested. If issues may be resolved through Examiner's Amendment, or clarified in any manner, a call to the undersigned attorney is respectfully requested.

Respectfully submitted,

Date: March 4, 2008

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